

**REMARKS**

Claims 1, 119-120, 122, 124-125, 127-129, 131-134, and 136-153 are pending in the application. The amendment to claim 132 was made to merely further clarify the presently claimed invention. No new matter has been added to the application.

**Rejection Under 35 U.S.C. §112, second paragraph**

Claims 132, 127, 129, 131, 134, 138-143, and 149-153 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant traverses this rejection. Reconsideration and withdrawal thereof are respectfully requested. However, Claim 132 has been amended. Accordingly, it is believed that this rejection has been overcome.

**Rejection Under 35 U.S.C. §103(a), (pp. 3-6), as being unpatentable over Sigal '670 (US 6,319,670), Burmer '149 (WO 99/45149), and/or Still '324 (USP 5,565,324)**

Claims 1, 119, 120, 124, 125, 127-129, 131-134, and 136-153 have been rejected under 35 U.S.C. §103(a) as being as being unpatentable over Sigal '670, Burmer '149, and/or Still '324. Applicant traverses this rejection. Reconsideration and withdrawal thereof are respectfully requested.

**Sigal '670**

Sigal '670 discloses methods, reagents and compositions for conducting electrochemiluminescence binding assays using microparticles that include electrically conductive material, which have one or more copies of an assay ligand immobilized on its outer surface and a plurality of electrochemiluminescent moieties immobilized on its outer surface, wherein the assay ligand is linked to the electrochemiluminescent moiety (Abstract). Sigal '670 also discloses attaching proteins to gold colloids (Examples 1 to 9, cols. 17 to 21).

However, Sigal '670 fails to disclose or suggest the presently claimed invention directed to immobilizing a protein species and a single sequence of oligonucleotide identifier independently on a common colloid particle surface, each on a different part of the surface to

participate in a chemical or biological interaction, wherein the protein species is immobilized on the surface via a self-assembled monolayer;  
allowing the interaction to occur while the protein species and the oligonucleotide identifier are immobilized on the common surface; and

determining participation of the protein species in the chemical or biological interaction by identifying the oligonucleotide identifier immobilized on the surface, comprising separating the oligonucleotide identifier from the surface and then identifying the oligonucleotide identifier, wherein the colloid particle is less than 500 nanometers cross section in any dimension.

In particular, Sigal '670 fails to disclose or suggest immobilizing a protein species on the surface of a self-assembled monolayer, as in the presently claimed invention. While Sigal '670 may suggest incorporating a "self-assembled monolayer" on a particle (col. 8, lines 8-21), Sigal '670 fails to provide an enabling disclosure for this assertion of coating a nanoparticle with SAM. A review of Examples I to VIII (Col 17, line 43 to Col. 20, line 67) shows anti-AFP antibody being "adsorbed" onto gold colloid without the use of any self-assembled monolayer. BSA-coated gold colloid is discussed in Example IV, however this can hardly be classified as a SAM coated gold colloid because BSA is not stable and does not fully coat the gold particle, and therefore is not useful for immobilizing protein species on the colloid particle.

It is well known that the size and type of surface is important in the chemical and physical reaction that would occur on the surfaces of planar substrate, microspheric bead and nanoparticle. Physical and chemical activity occurring on one of these types of surfaces is not necessarily predictive of same effects on the other type of surface. Applicant has for the first time determined a method of making nanoparticles that are coated with SAMs on to which proteins can be linked. In this regard, Sigal '670's mere suggestion that SAMs may be formed on a nanoparticle is unfounded, which is not based on any actual experimentation. Therefore, it is believed that Sigal '670 fails to be an enabling disclosure as against the presently claimed invention.

Moreover, Sigal '670 fails to disclose or suggest the use of an oligonucleotide tag to be placed on a common nanoparticle as the protein species. Sigal '670 fails to disclose or suggest

such a combination of molecules on a common nanoparticle. Accordingly, Sigal '670 is deficient in this regard against the presently claimed invention.

#### **Burmer '149**

Burmer '149 discloses making a hybrid DNA/protein molecule on a bead. Burmer '149 fails to disclose or suggest using a colloid particle in a method according to the presently claimed invention, in which a protein is connected to a colloid particle via SAM, and in which an identifier DNA is also connected to the colloid particle on a different part of the colloid particle to determine the interaction of the protein with another species. And because the Burmer '149 is directed to beads, which have chemically and physically distinct surfaces from nanoparticles, the Burmer '149 reference fails to be analogous art applicable to the presently claimed invention.

Moreover, since Burmer '149 fails to disclose or suggest using a self-assembled monolayer on a colloid, the Burmer '149 fails to remedy the deficiencies of the Sigal '670 reference to arrive at the presently claimed invention.

#### **Still '324**

Still '324 discloses combinatorial synthesis. Still '324 discloses a method of synthesizing small molecules or peptides on a bead.

Applicant submits that both of the Burmer '149 and Still '324 references are directed to step by step building of either a hybrid DNA/protein molecule or some other type of molecule on a bead. Neither Burmer '149 nor Still '324 discloses or suggests using colloid particle as a surface on which to place a single sequence identifier oligonucleotide and a protein on a common colloid surface on a different part of the common colloid particle as in the presently claimed invention. Therefore, the Burmer '149 and Still '324 references fail to be analogous art applicable to the presently claimed invention.

Applicant submits that the surface chemistry of a bead as disclosed in the Burmer '149 and Still '324 references is different from the surface chemistry of a nanoparticle such as a colloid. In addition, beads are "heavy" and therefore sink to the bottom of a reaction chamber. In contrast, a fluid suspendable nanoparticle, such as a colloid as in the presently claimed invention is not weighed down by gravity, which allows for a different type of chemical reaction to occur, which cannot be predicted from studies with beads. Moreover, the protein species taking part in

the biological or chemical interaction can be either covalently coupled to the colloid particle or through an affinity interaction on a self-assembled monolayer, which none of the prior art references discloses or suggests. In this regard, Still '324 fails to remedy the deficiencies of Burmer '149 in failing to disclose or suggest immobilizing a protein and a single sequence identifier oligonucleotide on a common colloid particle through self-assembled monolayer.

Moreover, since Still '324 fails to disclose or suggest using a self-assembled monolayer on a colloid, the Still '324 reference fails to remedy the deficiencies of the Sigal '670 reference to arrive at the presently claimed invention.

Accordingly, the presently claimed invention is not obvious over the cited references.

**Rejection Under 35 U.S.C. §103(a), (pp. 6-7), as being unpatentable over Sigal '670 (US 6,319,670), Burmer '149 (WO 99/45149), and/or Still '324 (USP 5,565,324) and further in view of Bamdad '839 (WO 98/31839)**

Claims 122 and 140 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Sigal '670, Burmer '149, and/or Still '324 and further in view of Bamdad '839. Applicant traverses this rejection. Reconsideration and withdrawal thereof are respectfully requested.

Sigal '670 is discussed above.

Burmer '149 is discussed above.

Still '324 is discussed above.

**Bamdad '839**

Bamdad '839 discloses a method of immobilizing biomolecules on a planar surface. Bamdad '839 discloses using surface plasmon resonance (SPR) to detect and analyze thin layers of material on a gold planar surface. Indeed, all of the examples at pages 40 to 64 are directed to making SPR type planar surfaces or chips on which are immobilized biological molecules. Bamdad '839 fails to disclose or suggest using colloidal molecules.

In view of the fact that experimental results obtained on planar surfaces cannot be predictive of results of using colloid particles, Applicants submit that Bamdad '839 fails to be combinable with the Sigal '670, Burmer '149 and Still '324, because a reference that discloses results on planar surfaces cannot be combined with results regarding large beads and

nanoparticles. Therefore, the presently claimed invention is not obvious over the cited references.

Applicant asserts that none of these references alone or in combination arrive at the presently claimed invention. The Burner '149 and Still '324 references disclose carrying out a synthesis reaction on beads. Bamdad '839 discloses carrying out a reaction on the gold surface of planar substrates and using surface plasmon resonance (SPR) to detect and analyze thin layers of material. Sigal '670 discloses using nanoparticles, but without any evidence that protein species may be formed on nanoparticles via SAMs. Further, none of these cited references discloses or suggests immobilizing a protein and a single sequence identifier oligonucleotide on a common colloid particle through self-assembled monolayer. Accordingly, the presently claimed invention is not obvious over the cited references.

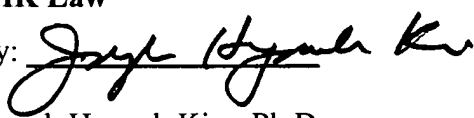
### **Conclusion**

It is believed that the application is now in condition for allowance. Applicants request the Examiner to issue a notice of Allowance in due course. The Examiner is encouraged to contact the undersigned to further the prosecution of the present invention.

The Commissioner is authorized to charge JHK Law's Deposit Account No. **502486** for any fees required under 37 CFR § 1.16 and 1.17 and to credit any overpayment to said Deposit Account No. **502486**.

Respectfully submitted,

**JHK Law**

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